SEQUENCE LISTING

<110> Ludmerer, Steven W.
Graham, Donald J.
LaFemina, Robert L.
Flores, Osvaldo A.
Pizzuti, Maura
Traboni, Cinzia

<120> HCV REPLICONS CONTAINING NS5B FROM GENOTYPE 2B

<130> 21564YP

<140> 10/577,893
<141> 2006-05-01

<150> PCT/US2004/036575
<151> 2004-11-03

<150> 60/517,605
<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 591
<212> PRT
<213> Artificial Sequence

<220>
<223> modified NS5B

<221> VARIANT
<222> (5)...(5)
<223> Xaa = threonine or serine

<221> VARIANT
<222> (24)...(24)
<223> Xaa = asparagine or serine

<221> VARIANT
<222> (31)...(31)
<223> Xaa = methionine or isoleucine

<221> VARIANT
<222> (392)...(392)
<223> Xaa = isoleucine or leucine

<400> 1

Ser	Met	Ser	Tyr	Xaa	Trp	Thr	Gly	Ala	Leu	Ile	Thr	Pro	Cys	Gly	Pro
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            20                  25                  30
Phe His Asn Lys Val Tyr Ser Thr Thr Ser Arg Ser Ala Ser Leu Arg
        35                  40                  45
Ala Lys Lys Val Thr Phe Asp Arg Val Gln Val Leu Asp Ala His Tyr
    50                  55                  60
Asp Ser Val Leu Gln Asp Val Lys Arg Ala Ala Ser Lys Val Ser Ala
65                  70                  75                  80
Arg Leu Leu Thr Val Glu Glu Ala Cys Ala Leu Thr Pro Pro His Ser
                85                  90                  95
Ala Lys Ser Arg Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu Ser
            100                 105                 110
Arg Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu Glu
        115                 120                 125
Asp Gln His Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val
    130                 135                 140
Phe Cys Ile Asp Pro Thr Lys Gly Gly Lys Lys Pro Ala Arg Leu Ile
145                 150                 155                 160
Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr
                165                 170                 175
Asp Ile Ala Gln Lys Leu Pro Lys Ala Ile Met Gly Pro Ser Tyr Gly
            180                 185                 190
Phe Gln Tyr Ser Pro Ala Glu Arg Val Asp Phe Leu Leu Lys Ala Trp
        195                 200                 205
Gly Ser Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe
    210                 215                 220
Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr
225                 230                 235                 240
Gln Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu
                245                 250                 255
Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn Ser Lys Gly Gln
            260                 265                 270
Ser Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser
        275                 280                 285
Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys
    290                 295                 300
Ala Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu
305                 310                 315                 320
Val Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu
                325                 330                 335
Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
            340                 345                 350
Leu Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
        355                 360                 365
Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Arg Tyr Phe Leu
    370                 375                 380
Thr Arg Asp Pro Thr Thr Pro Xaa Thr Arg Ala Ala Trp Glu Thr Val
385                 390                 395                 400
Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr Ala
                405                 410                 415
Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser Ile
            420                 425                 430
Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met Tyr
        435                 440                 445
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Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu
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Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His
465                 470                 475                 480
Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro
                485                 490                 495
Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
            500                 505                 510
Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
        515                 520                 525
Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
    530                 535                 540
Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Gly Asp Ile
545                 550                 555                 560
Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Leu Cys Leu
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Leu Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
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<211> 1776
<212> DNA
<213> Artificial Sequence

<220>
<223> modified NS5B

<221> variation
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<223> n = A or T

<221> variation
<222> (9)...(9)
<223> n = C or A

<221> variation
<222> (13)...(13)
<223> n = A or T

<221> variation
<222> (15)...(15)
<223> n = A or C

<221> variation
<222> (21)...(21)
<223> n - A or G

<221> variation
<222> (24)...(24)
<223> n = C or G

<221> variation
<222> (28)...(28)
<223> n = T or C

<221> modified_base
<222> (30)...(30)
<223> n = G or C

<221> variation
<222> (33)...(33)
<223> n = C or A

<221> variation
<222> (71)...(71)
<223> n = A or G

<221> variation
<222> (83)...(83)
<223> n = G or T

<221> variation
<222> (1174)...(1174)
<223> n = A or C

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acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacagggt gcaggtgctg 180
gacgcacact atgactcagt cttgcaggac gttaagcggg ccgcctctaa ggttagtgcg 240
aggctcctca cggtagagga agcctgcgcg ctgaccccgc cccactccgc caaatcgcga 300
tacggatttg gggcaaaaga ggtgcgcagc ttatctagga gggccgttaa ccacatccgg 360
tccgtgtggg aggacctcct ggaagaccaa catacccaa ttgacacaac tatcatggct 420
aaaaatgagg tgttctgcat tgatccaact aaaggtggga aaaagccagc tcgcctcatc 480
gtataccccg accttggggt cagggtgtgc gaaaagatgg ccctctatga catcgcacaa 540
aagcttccca aagcgataat ggggccatcc tatgggttcc aatactctcc cgcagaacgg 600
gtcgatttcc tcctcaaagc ttggggaagt aagaaggacc caatggggtt ctcgtatgac 660
acccgctgct ttgactcaac cgtcacggag agggacataa gaacagaaga atccatatat 720
caggcttgtt ctctgcctca agaagccaga actgtcatac actcgctcac tgagagactt 780
tacgtaggag ggcccatgac aaacagcaaa gggcaatcct gcggctacag gcgttgccgc 840
gcaagcggtg ttttcaccac cagcatgggg aataccatga catgttacat caaagcccct 900
gcagcgtgta aggctgcagg gatcgtggac cctgttatgt tggtgtgtgg agacgacctg 960
gtcgtcatct cagagagcca aggtaacgag gaggacgagc gaaacctgag agctttcacg 1020
gaggctatga ccaggtattc cgcccctccc ggtgaccttc ccagaccgga atatgacttg 1080
gagcttataa catcctgctc ctcaaacgta tcggtagcgc tggactctcg gggtcgccgc 1140
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caaaatctca attttgagat gtacggggca gtatactcgg tcaatccatt agacctaccg 1380
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aagagtcggg cgcgtgccgt gagagcttca ctcatcgccc aaggagcgag ggcggccatt 1560
tgtggccgct acctcttcaa ctgggcggtg aaaacaaagc tcaaactcac tccattgccc 1620
gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg gcgccggcgg gggcgacatt 1680
tatcacagcg tgtcgcatgc ccgaccccgc ctattactcc tttgcctact cctacttagc 1740
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<210> 3
<211> 1394
<212> PRT

<213> Artificial Sequence

<220>
<223> modified NS3-5A

<221> VARIANT
<222> (1215)...(1215)
<223> Xaa = asparagine or serine

<221> VARIANT
<222> (904)...(904)
<223> Xaa = valine or alanine

<400> 3

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			20					25					30		
Glu	Val	Gln	Val	Val	Ser	Thr	Ala	Thr	Gln	Ser	Phe	Leu	Ala	Thr	Cys
		35					40					45			
Val	Asn	Gly	Val	Cys	Trp	Thr	Val	Tyr	His	Gly	Ala	Gly	Ser	Lys	Thr
	50					55					60				
Leu	Ala	Gly	Pro	Lys	Gly	Pro	Ile	Thr	Gln	Met	Tyr	Thr	Asn	Val	Asp
65					70					75					80
Gln	Asp	Leu	Val	Gly	Trp	Gln	Ala	Pro	Pro	Gly	Ala	Arg	Ser	Leu	Thr
				85					90					95	
Pro	Cys	Thr	Cys	Gly	Ser	Ser	Asp	Leu	Tyr	Leu	Val	Thr	Arg	His	Ala
			100					105					110		
Asp	Val	Ile	Pro	Val	Arg	Arg	Arg	Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu
		115					120					125			
Ser	Pro	Arg	Pro	Val	Ser	Tyr	Leu	Lys	Gly	Ser	Ser	Gly	Gly	Pro	Leu
	130					135					140				
Leu	Cys	Pro	Ser	Gly	His	Ala	Val	Gly	Ile	Phe	Arg	Ala	Ala	Val	Cys
145					150					155					160
Thr	Arg	Gly	Val	Ala	Lys	Ala	Val	Asp	Phe	Val	Pro	Val	Glu	Ser	Met
				165					170					175	
Glu	Thr	Thr	Met	Arg	Ser	Pro	Val	Phe	Thr	Asp	Asn	Ser	Ser	Pro	Pro
			180					185					190		
Ala	Val	Pro	Gln	Thr	Phe	Gln	Val	Ala	His	Leu	His	Ala	Pro	Thr	Gly
		195					200					205			
Ser	Gly	Lys	Ser	Thr	Lys	Val	Pro	Ala	Ala	Tyr	Ala	Ala	Gln	Gly	Tyr
	210					215					220				
Lys	Val	Leu	Val	Leu	Asn	Pro	Ser	Val	Ala	Ala	Thr	Leu	Gly	Phe	Gly
225					230					235					240
Ala	Tyr	Met	Ser	Lys	Ala	His	Gly	Ile	Asp	Pro	Asn	Ile	Arg	Thr	Gly
				245					250					255	
Val	Arg	Thr	Ile	Thr	Thr	Gly	Ala	Pro	Val	Thr	Tyr	Ser	Thr	Tyr	Gly
			260					265					270		
Lys	Phe	Leu	Ala	Asp	Gly	Gly	Cys	Ser	Gly	Gly	Ala	Tyr	Asp	Ile	Ile
		275					280					285			
Ile	Cys	Asp	Glu	Cys	His	Ser	Thr	Asp	Ser	Thr	Thr	Ile	Leu	Gly	Ile
	290					295					300				
Gly	Thr	Val	Leu	Asp	Gln	Ala	Glu	Thr	Ala	Gly	Ala	Arg	Leu	Val	Val
305					310					315					320

```
Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
                  325                 330                 335
Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
              340                 345                 350
Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
          355                 360                 365
Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
      370                 375                 380
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
385                 390                 395                 400
Ile Pro Thr Ile Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met
                  405                 410                 415
Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
              420                 425                 430
Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
          435                 440                 445
Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly
      450                 455                 460
Arg Thr Gly Arg Gly Arg Met Gly Ile Tyr Arg Phe Val Thr Pro Gly
465                 470                 475                 480
Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
                  485                 490                 495
Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val
              500                 505                 510
Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
          515                 520                 525
His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp
      530                 535                 540
Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr
545                 550                 555                 560
Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
                  565                 570                 575
Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
              580                 585                 590
Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
          595                 600                 605
Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met
      610                 615                 620
Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly
625                 630                 635                 640
Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val
                  645                 650                 655
Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp
              660                 665                 670
Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser
          675                 680                 685
His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys
      690                 695                 700
Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala
705                 710                 715                 720
Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp
                  725                 730                 735
Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly
              740                 745                 750
```

```
Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe
        755                 760                 765
Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe
    770                 775                 780
Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala
785                 790                 795                 800
Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser
                805                 810                 815
Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala
            820                 825                 830
Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met
        835                 840                 845
Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro
    850                 855                 860
Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His
865                 870                 875                 880
Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala
                885                 890                 895
Phe Ala Ser Arg Gly Asn His Xaa Ser Pro Thr His Tyr Val Pro Glu
            900                 905                 910
Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile
        915                 920                 925
Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser
    930                 935                 940
Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys
945                 950                 955                 960
Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro
                965                 970                 975
Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly
            980                 985                 990
Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala
        995                 1000                1005
Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro
    1010                1015                1020
Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr
1025                1030                1035                1040
Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala
                1045                1050                1055
Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly
            1060                1065                1070
Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro
        1075                1080                1085
Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg
    1090                1095                1100
Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val
1105                1110                1115                1120
Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro
                1125                1130                1135
Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp
            1140                1145                1150
Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly
        1155                1160                1165
Ser Pro Pro Ser Leu Ala Ser Ser Ser Ala Ile Gln Leu Ser Ala Pro
    1170                1175                1180
```

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Ser Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp
1185                1190                1195                1200
Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Xaa Ile
                1205                1210                1215
Thr Arg Val Glu Ser Glu Asn Lys Val Val Val Leu Asp Ser Phe Asp
            1220                1225                1230
Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu
        1235                1240                1245
Ile Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala
    1250                1255                1260
Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp
1265                1270                1275                1280
Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala
                1285                1290                1295
Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
            1300                1305                1310
Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly
        1315                1320                1325
Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro
    1330                1335                1340
Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr
1345                1350                1355                1360
Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser
                1365                1370                1375
Asp Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val
            1380                1385                1390
Cys Cys
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<210> 4
<211> 4182
<212> DNA
<213> Artificial Sequence

<220>
<223> modified NS3-5A

<221> variation
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<223> n = T or C

<221> variation
<222> (3645)...(3645)
<223> n = A or G

<400> 4

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gcccaagggt acaaggtgct cgtcctcaat ccgtccgttg ccgctacctt agggtttggg 720
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Cys	Ser	Thr	Pro	Cys											
				260											